

AMENDMENTS TO THE SPECIFICATION

Please replace the title with the following amended title:

NOVEL AMINO ACID DERIVATIVES AND PHARMACEUTICAL USES
THEREOF ~~COMPOUNDS AND METHODS OF USING THE SAME~~

Please replace the first paragraph after the title (added by preliminary amendment) with the following further amended paragraph:

CROSS REFERENCE TO RELATED APPLICATIONS

This application is the National Stage of International Application No. PCT/GB2004/002569, filed June 16, 2004, which claims the benefit of British ~~Britis~~ Patent Application Serial No. 2003-0314262.7, filed on June 19, 2003. The contents of both of which are hereby incorporated by reference in their entireties.

Please insert the following heading on page 24 prior to the paragraph beginning at line 6, as shown below, along with said paragraph:

Brief Description of the Figures

Figure 1 shows a synthesis route for the production of an exemplary compound according to the first aspect of the invention, namely *N*-Benzyloxycarbonyl-*L*-phenylalanyl-6-dimethylsulfonium-5-oxo-*L*-norleucine bromide salt ('Compound 281'). In step (i) the *N*- α -CBZ-protected amino acid *N*-hydroxysuccinimide ester is reacted with 6-diazo-5-oxo-*L*-norleucine (DON) to produce *Z*-phenylalaninyl bromomethyl ketone, which is then reacted with dimethylsulphide to produce *N*-benzyloxycarbonyl-*L*-phenylalanyl-6-dimethylsulfonium-5-oxo-*L*-norleucine bromide salt.

Please replace the paragraph on page 29, beginning at line 1, with the following amended paragraph:

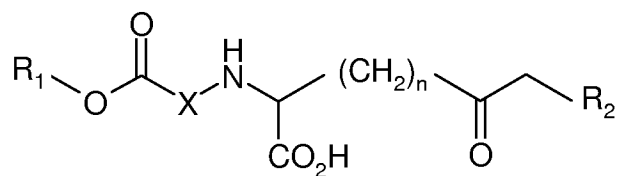
Figure 26 (a and b) shows the effect on renal function in rats of 84 days treatment with the inhibitors *N*-Benzyloxycarbonyl-*L*-phenylalanyl-6-di-methylsulfonium-5-oxo-*L*-norleucine bromide salt (designated 'SNx + 281') and 1,3-dimethyl-2-(2-oxopropylsulfanyl)-3H-1,3-diazol-1-ium-chloride (designated 'SNx + 283'), as determined using measurements of: Figure 26(a) proteinuria and Figure 26(b) creatinine clearance. 'SNc' refers to control kidneys obtained from animals on which a sham operation was performed without subtotal nephrectomy. 'SNx' refers to subtotal nephrectomy. Five animals per group were used (see Example 4).

Please replace the abstract with the following amended abstract:

ABSTRACT

Novel Amino Acid Derivatives ~~compounds~~ and Pharmaceutical Uses Thereof ~~methods~~
of using the same

~~The present invention relates to~~ Provided are novel compounds of Formula I:



wherein 'X' represents an amino acid group, 'n' is an integer between 1 and 4, 'R₁' represents benzyl, t-butyl or 9-fluorenylmethyl and 'R₂' represents a tetramethylmercaptoimidazole derivative or -S⁺R₃R₄, wherein R₃ and R₄ each independently represent lower alkyl, or a pharmaceutically and/or veterinarily acceptable derivative thereof. ~~The present invention further relates to~~ Further provided are pharmaceutical formulations of ~~said compound~~ the compounds and

the use thereof in the preparation of a medicament for inhibiting diseases in which transglutaminase has been implicated. Advantageously, the medicament is for treating fibrosis, scarring and/or cancer. Additionally provided are methods, ~~the invention relates to a method~~ of inhibiting autoimmune diseases such as coeliac disease, neurodegeneration and chronic inflammatory diseases (e.g. of the joints including rheumatoid arthritis and osteoarthritis in a subject). ~~The invention further relates to~~ and a method for preventing or treating rejection of a transplanted organ.